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Application No.: 10/623065 Docket No.: BPI-190

In the claims:

Please amend claims 1-3, 7-12, 15-16, and 25-26.

1. **(Currently amended)** A method of treating or preventing a coronary disorder in a subject comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, such that the coronary disorder is treated or prevented.

2. **(Currently amended)** A method of treating or preventing a coronary disorder in a subject comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that said coronary disorder is treated or prevented.

3. **(Currently amended)** A method of treating or preventing a coronary disorder in a subject comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that said coronary disorder is treated or prevented.

4. **(Original)** The method of any one of claims 1, 2, and 3, wherein the antibody, or antigen-binding fragment thereof, is D2E7.

5. **(Original)** The method of any one of claims 1, 2, and 3, wherein the coronary disorder is restenosis.

6. **(Original)** The method of any one of claims 1, 2, and 3, wherein the coronary disorder is selected from the group consisting of acute congestive heart failure, an acute coronary syndrome (including angina and myocardial infarction), antherosclerosis, chronic antherosclerosis, cardiomyopathy, congestive heart failure (chronic and acute), and rheumatic heart disease.

7. **(Currently amended)** A method of treating or preventing restenosis in a subject comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, such that said restenosis is treated or prevented.

8. **(Currently amended)** A method of treating or preventing restenosis in a subject comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9,

10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12, such that said restenosis is treated or prevented.

9. **(Currently amended)** A method of treating or preventing restenosis in a subject comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2, such that said restenosis is treated or prevented.

10. **(Currently amended)** The method of any one of claims 7, 8, or 9, wherein the ~~TNFα~~ antibody, or antigen binding fragment thereof, is D2E7.

11. **(Currently amended)** The method of any one of claims 7, 8, or 9, wherein the ~~TNFα~~ antibody is administered with at least one additional therapeutic agent.

12. **(Currently amended)** A method for inhibiting human TNFα activity in a human subject suffering from a coronary disorder comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

13. **(Original)** The method of claim 12, wherein the coronary disorder is restenosis.

14. **(Original)** The method of claim 12, wherein the coronary disorder is selected from the group consisting of acute congestive heart failure, an acute coronary syndrome (including angina and myocardial infarction), artherosclerosis, chronic artherosclerosis, cardiomyopathy, congestive heart failure (chronic and acute), and rheumatic heart disease.

15. **(Currently amended)** The method of any one of claims 12, 13, and 14, wherein the ~~TNFα~~ antibody, or antigen-binding fragment thereof, is D2E7.

16. **(Currently amended)** A method for inhibiting human TNFα activity in a human subject suffering from restenosis, comprising administering a therapeutically effective amount of a human ~~TNFα~~ antibody, or an antigen-binding fragment thereof, to the subject, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

17. **(Original)** The method of claim 16, wherein the antibody, or antigen binding fragment thereof, is D2E7.

18. **(Original)** A method of treating or preventing a coronary disorder in a subject comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that the coronary disorder is treated or prevented.

19. **(Original)** The method of claim 18, wherein the coronary disorder is restenosis.

20. **(Original)** The method of claim 18, wherein the coronary disorder is selected from the group consisting of acute congestive heart failure, an acute coronary syndrome (including angina and myocardial infarction), artherosclerosis, chronic artherosclerosis, cardiomyopathy, congestive heart failure (chronic and acute), and rheumatic heart disease.

21. **(Original)** A method of treating a subject suffering from restenosis comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, to the subject, such that said restenosis is treated.

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~~22~~ 23. **(Original)** A method of treating a subject suffering from or at risk of developing restenosis comprising administering a therapeutically effective amount of D2E7, or an antigen-binding fragment thereof, and at least one additional therapeutic agent to the subject, such that the coronary disorder is treated.

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23 ~~24~~. **(Original)** The method of claim 23, wherein the additional therapeutic agent is selected from the group consisting of sirolimus, paclitaxel, everolimus, tacrolimus, ABT-578, and acetaminophen.

24 ~~25~~. **(Currently amended)** A kit comprising:

a) a pharmaceutical composition comprising a human ~~TNFα~~ antibody, or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less; and

b) instructions for administering to a subject the ~~TNFα~~ antibody pharmaceutical composition for treating a subject who is suffering from a coronary disorder.

25 ~~26~~. **(Currently amended)** A kit according to claim 23, wherein the ~~TNFα~~ antibody, or an antigen binding portion thereof, is D2E7.